# nature research

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# **Reporting Summary**

Nature Research wishes to improve the reproducibility of the work that we publish. This form provides structure for consistency and transparency in reporting. For further information on Nature Research policies, see our Editorial Policies and the Editorial Policy Checklist.

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St	· a	t١	c†	ICC

Fora	all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.
n/a	Confirmed
	$oxed{x}$ The exact sample size (n) for each experimental group/condition, given as a discrete number and unit of measurement
	🕱 A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
	The statistical test(s) used AND whether they are one- or two-sided Only common tests should be described solely by name; describe more complex techniques in the Methods section.
×	A description of all covariates tested
×	A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
	A full description of the statistical parameters including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)
	For null hypothesis testing, the test statistic (e.g. <i>F</i> , <i>t</i> , <i>r</i> ) with confidence intervals, effect sizes, degrees of freedom and <i>P</i> value noted <i>Give P values as exact values whenever suitable.</i>
×	For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
X	For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
x	Estimates of effect sizes (e.g. Cohen's <i>d</i> , Pearson's <i>r</i> ), indicating how they were calculated
	Our web collection on <u>statistics for biologists</u> contains articles on many of the points above.
So.	ftware and code

Data analysis (HKL2000, CCP 4 6.5, Coot 0.8.2, PHENIX-1.10.1, PyMOL 2.4.0, Graphpad prism 8.0.2, Phaser 2.8.3, MolProbity 4.2, FlowJo 10.0.7

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors and reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Research guidelines for submitting code & software for further information.

Diffraction data were collected at Shanghai Synchrotron Radiation Facility (SSRF) beamline BL18U1.

#### Data

Data collection

Policy information about availability of data

All manuscripts must include a data availability statement. This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A list of figures that have associated raw data
- A description of any restrictions on data availability

Policy information about availability of computer code

Atomic coordinates and structure factors have been deposited in the Protein Data Bank under the accession code 7E3J (https://www.rcsb.org/structure/7E3J). Raw data for Fig. 1, 4, 5, and Supplementary Figure 1 are available in the source data file. Other data are available from the corresponding authors upon reasonable request.

#### Field-specific reporting

Ple	ease select the one below	that	t is the best fit for your research. If	yo	u are not sure, read the appropriate sections before making your selection.
X	Life sciences		Behavioural & social sciences		Ecological, evolutionary & environmental sciences

For a reference copy of the document with all sections, see <u>nature.com/documents/nr-reporting-summary-flat.pdf</u>

## Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

Sample size The experiments in fig. 1d & 1e, fig 4d & 4h, Suppl. Figure 1 were performed with triplicate, quadruplicate or cell samples. Student's t-test was used to detect the statistic significant. The sample size of n>=3 is a general principle used for cell experiments.

Data exclusions No data were excluded from the analyses

Replication Biochemical experiments were each replicated at least three times. We confirm that all attempts at replication were successful.

Randomization Randomization was not relevant to our study. Because there's no allocation of samples/organisms/participants involved in our study.

Blinding was not relevant to our study. Because there's no group allocation involved in this study.

## Behavioural & social sciences study design

All studies must disclose on these points even when the disclosure is negative.

T studies must disclose on these points even when the disclosure is negative.

Briefly describe the study type including whether data are quantitative, qualitative, or mixed-methods (e.g. qualitative cross-sectional, quantitative experimental, mixed-methods case study).

Research sample

State the research sample (e.g. Harvard university undergraduates, villagers in rural India) and provide relevant demographic information (e.g. age, sex) and indicate whether the sample is representative. Provide a rationale for the study sample chosen. For studies involving existing datasets, please describe the dataset and source.

Describe the sampling procedure (e.g. random, snowball, stratified, convenience). Describe the statistical methods that were used to predetermine sample size OR if no sample-size calculation was performed, describe how sample sizes were chosen and provide a rationale for why these sample sizes are sufficient. For qualitative data, please indicate whether data saturation was considered, and

what criteria were used to decide that no further sampling was needed.

Data collection Provide details about the data collection procedure, including the instruments or devices used to record the data (e.g. pen and paper, computer, eye tracker, video or audio equipment) whether anyone was present besides the participant(s) and the researcher, and

whether the researcher was blind to experimental condition and/or the study hypothesis during data collection.

Timing Indica

Indicate the start and stop dates of data collection. If there is a gap between collection periods, state the dates for each sample cohort.

Data exclusions

Blinding

Study description

If no data were excluded from the analyses, state so OR if data were excluded, provide the exact number of exclusions and the rationale behind them, indicating whether exclusion criteria were pre-established.

Non-participation

State how many participants dropped out/declined participation and the reason(s) given OR provide response rate OR state that no participants dropped out/declined participation.

Randomization

If participants were not allocated into experimental groups, state so OR describe how participants were allocated to groups, and if allocation was not random, describe how covariates were controlled.

## Ecological, evolutionary & environmental sciences study design

All studies must disclose on these points even when the disclosure is negative.

Study description

Briefly describe the study. For quantitative data include treatment factors and interactions, design structure (e.g. factorial, nested, hierarchical), nature and number of experimental units and replicates.

Research sample

Describe the research sample (e.g. a group of tagged Passer domesticus, all Stenocereus thurberi within Organ Pipe Cactus National Monument), and provide a rationale for the sample choice. When relevant, describe the organism taxa, source, sex, age range and any manipulations. State what population the sample is meant to represent when applicable. For studies involving existing datasets, describe the data and its source.

Sampling strategy	Note the sampling procedure. Describe the statistical methods that were used to predetermine sample size OR if no sample-size calculation was performed, describe how sample sizes were chosen and provide a rationale for why these sample sizes are sufficient.				
Data collection	Describe the data collection procedure, including who recorded the data and how.				
Timing and spatial scale	Indicate the start and stop dates of data collection, noting the frequency and periodicity of sampling and providing a rationale for these choices. If there is a gap between collection periods, state the dates for each sample cohort. Specify the spatial scale from which the data are taken				
Data exclusions	If no data were excluded from the analyses, state so OR if data were excluded, describe the exclusions and the rationale behind them, indicating whether exclusion criteria were pre-established.				
Reproducibility	Describe the measures taken to verify the reproducibility of experimental findings. For each experiment, note whether any attempts to repeat the experiment failed OR state that all attempts to repeat the experiment were successful.				
Randomization	Describe how samples/organisms/participants were allocated into groups. If allocation was not random, describe how covariates were controlled. If this is not relevant to your study, explain why.				
Blinding	Describe the extent of blinding used during data acquisition and analysis. If blinding was not possible, describe why OR explain why blinding was not relevant to your study.				
Did the study involve field	d work? Yes 🗷 No				
Field work collec	tion and transport				
Field conditions	Describe the study conditions for field work, providing relevant parameters (e.g. temperature, rainfall).				
Location	State the location of the sampling or experiment, providing relevant parameters (e.g. latitude and longitude, elevation, water depth).				
Access & import/export	Describe the efforts you have made to access habitats and to collect and import/export your samples in a responsible manner and in compliance with local, national and international laws, noting any permits that were obtained (give the name of the issuing authority, the date of issue, and any identifying information).				
Disturbance	Describe any disturbance caused by the study and how it was minimized.				
We require information from a	or specific materials, systems and methods authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, evant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.				
Materials & experime	ental systems Methods				
n/a Involved in the study	n/a Involved in the study				
Antibodies	ChIP-seq				
Eukaryotic cell lines  Palaeontology and a					
Animals and other organisms					
Human research participants					
Clinical data					
<b>x</b> Dual use research o	f concern				
Antibodies					
Antibodies used	Anti-His-APC (Supplier: Miltenyi Biotec; catalog number: 130-119-782; clone name: GG11-8F3.5.1; lot number: 5200401441)				
Validation	Describe the validation of each primary antibody for the species and application, noting any validation statements on the manufacturer's website, relevant citations, antibody profiles in online databases, or data provided in the manuscript.				
Eukaryotic cell lin	es				
Policy information about ce					
Toncy initiation about Ce	an inica				

Authentication

No

Mycoplasma contamination	We have confirmed that there is no Mycoplasma in our cells.
Commonly misidentified lines (See ICLAC register)	No

#### Flow Cytometry

#### **Plots**

Confirm that:

- The axis labels state the marker and fluorochrome used (e.g. CD4-FITC).
- The axis scales are clearly visible. Include numbers along axes only for bottom left plot of group (a 'group' is an analysis of identical markers).
- 🗶 All plots are contour plots with outliers or pseudocolor plots.
- 🗶 A numerical value for number of cells or percentage (with statistics) is provided.

#### Methodology

For flow cytometry analysis, BHK cells were transfected with the full length dACE2 and hACE2 fused with eGFP and incubated in 5% CO2 at 37°C for 48 h. Then, cells were resuspended, collected and incubated with RBD or MERS-CoV RBD proteins of a concentration of 5 µg/mL at 37 °C for 30 min. After that, the cells were washed three times with PBS and stained by anti-His/APC antibody (1:500, Miltenyi Biotec) at 37 °C. After 30 min incubation, the cells were washed three times with PBS.

Instrument BD FACSCanto

Software FlowJo 10.0

Cell population abundance 2 million cells

Gating strategy eGFP-positive BHK Cells are gated first, followed by analysis of anti-his-APC positive cells

| Tick this box to confirm that a figure exemplifying the gating strategy is provided in the Supplementary Information.